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10/506,665	09/07/2004	Beka Solomon	SOLOMON6A	5010

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EXAMINER

EMCH, GREGORY S

ART UNIT	PAPER NUMBER
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1649

MAIL DATE	DELIVERY MODE
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01/17/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/506,665	<b>Applicant(s)</b> SOLOMON, BEKA	
	<b>Examiner</b> Gregory S. Emch	<b>Art Unit</b> 1649	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-15,27,29,38,40 and 42-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15,42 and 44-50 is/are rejected.
- 7) ☒ Claim(s) 27,29,38,40 and 43 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

The examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Gregory S. Emch, Art Unit 1649.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01 October 2007 has been entered.

#### ***Response to Amendment***

Claims 1, 2, 4, 5, 11, 13, 14, 27, 29, 38 and 40 have been amended, claims 23-26, 28, 30-37, 39 and 41 have been canceled and new claims 42-50 have been added as requested in the amendment filed on 01 October 2007. Following the amendment, claims 1-15, 27, 29, 38, 40 and 42-50 are pending in the instant application.

Claims 1-15, 27, 29, 38, 40 and 42-50 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 1-3, 5-10 and 15 under nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 6, 10, 16-17 and 21-24 of copending Application No. 10/481,642 ('642 application) is maintained for reasons of record. Furthermore, newly presented claims 44-47, 49 and 50 are also subject to the instant double patenting rejection.

In the reply filed on 01 October 2007, Applicant asserts, "The invention of copending application '642 is directed to antigenic products that display epitopes of deposit-forming polypeptide such as amyloid  $\beta$ . Accordingly, the claims of '642 only superficially overlap with the instant claims because the antigenic peptide recited in '642 may optionally include residues other than, e.g., those in an epitope of amyloid  $\beta$ . Likewise, the antigenic peptide recited in the instant claims may optionally include the EFRH epitope of amyloid  $\beta$  that is a preferred amyloid  $\beta$  epitope in '642. However, both are primarily directed to different epitopes, amyloid  $\beta$  versus the  $\beta$ -secretase cleavage site which is not present in amyloid  $\beta$ ."

Applicant's arguments have been fully considered but they are not persuasive. The claims of copending application 10/481,642 have been amended in the reply filed on 15 November 2007 and are now directed to an antigenic product comprising an antigenic peptide "that comprises an epitope of amyloid  $\beta$  comprising the amino acid

sequence of SEQ ID NO: 5". SEQ ID NO: 5 of the '642 application is the sequence EFRH. Thus, contrary to Applicant's assertion, the claims of the '642 application do not "only superficially overlap with the instant claims" since the claims of the '642 application require the amino acid sequence of EFRH. This is evidenced by instant claim 5, for example, which recites that the A $\beta$ PP epitope spanning the  $\beta$ -secretase cleavage site of A $\beta$ PP comprises SEQ ID NO: 5, which is the sequence VKMDAEFRH. This epitope *comprises* the epitope of the claims of the '642 application (EFRH). Thus, the claims are not directed to primarily different epitopes. Applicant is reminded that the claims of both cases recite the open language "comprising," which does not exclude additional unrecited elements (see MPEP 2111.03). Moreover, as stated previously, the skilled artisan would recognize that administration of an immunizing composition comprising VKMDAEFRH would produce a polyclonal antibody response comprising antibodies directed not only to the  $\beta$ -secretase cleavage site as instantly claimed, but also to the highly antigenic portion of amyloid  $\beta$ , particularly the EFRH epitope. Thus, the claims of the co-pending applications are considered obvious variants and the rejection is maintained.

The rejection of claims 11, 12 and 14 under the doctrine of provisional nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 and 10 of copending Application No. 11/073,526 ('526 application) is maintained for reasons of record.

In the reply filed on 01 October 2007, Applicant asserts, "Similar to the argument presented above, '526 is directed to a virus particle displaying a peptide which includes epitopes of amyloid  $\beta$  to induce an immune response to amyloid  $\beta$ . Such a virus particle may optionally include other residues besides those in an epitope of amyloid  $\beta$ .

However, any such additional residues would include the  $\beta$ -secretase cleavage site merely by coincidence and not by design. Thus, one of ordinary skill in the art would not be motivated to specifically include residues from the  $\beta$ -secretase cleavage site in A $\beta$ PP that are not present in amyloid  $\beta$  on a virus particle (to be displayed with the amyloid  $\beta$  epitope) when the goal of '526 is to elicit an immune response against the amyloid  $\beta$  target, not the  $\beta$ -secretase cleavage site of A $\beta$ PP."

Applicant's arguments have been fully considered but they are not persuasive. The claims of the '526 application are directed to an antigenic virus particle displaying a polypeptide, wherein said polypeptide *comprises* at least one epitope of amyloid  $\beta$ . Thus, the polypeptide is not limited to epitopes contained only within amyloid  $\beta$ . Also, as noted above, the A $\beta$ PP molecule comprises the amyloid  $\beta$  polypeptide, such that the species of antigenic peptide recited in claim 10 of the '526 application, namely an epitope comprising EFRH, would anticipate the genus of antigenic molecules instantly claimed, which comprises such an amyloid  $\beta$  epitope. Therefore, Applicant's assertion, "any such additional residues would include the  $\beta$ -secretase cleavage site is merely by coincidence and not by design" is irrelevant and the claims of the co-pending applications are considered obvious variants. Accordingly, the instant double patenting rejection is maintained.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 44-50 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are directed to an antigenic peptide consisting of 6-14 amino acid residues of the amyloid precursor protein (A $\beta$ PP) that span the  $\beta$ -secretase cleavage site of A $\beta$ PP.

The claims, as written, do not sufficiently distinguish the claimed invention over proteins that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor by insertion of "isolated" or "purified," for example. See MPEP 2105.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and



the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-11, 13-15, 42, 44-46 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/72880 A2 to Schenk et al.

Claims 1-11, 13, 14 and 42 are directed to an immunizing composition, comprising an immunizing effective amount of an antigenic product which induces an immune response against the  $\beta$ -secretase cleavage site of amyloid precursor protein (A $\beta$ PP) and a pharmaceutically acceptable carrier, diluent, excipient, adjuvant, or auxiliary agent, wherein said antigenic product comprises a display vehicle and an antigenic peptide displayed on said display vehicle, said antigenic peptide comprising a 6-14 amino acid residue A $\beta$ PP epitope that spans the  $\beta$ -secretase cleavage site of A $\beta$ PP. Claim 15 is directed to a method for inducing an immune response against the  $\beta$ -secretase cleavage site of A $\beta$ PP comprising administering the immunizing composition of claim 1 to a human subject in need thereof to induce an immune response against the  $\beta$ -secretase cleavage site of A $\beta$ PP and block  $\beta$ -secretase cleavage of A $\beta$ PP, thereby inhibiting the formation of amyloid  $\beta$ . Claims 44-46 and 49

are directed to an antigenic peptide consisting of 6-14 amino acid residues of the amyloid precursor protein (A $\beta$ PP) that span the  $\beta$ -secretase cleavage site of A $\beta$ PP.

Upon reading the disclosure of the '880 document, the skilled artisan would have recognized the desirability of developing improved products or compositions for methods of treating or preventing a disease associated with amyloid deposits of A $\beta$  in the brain of a patient, such as Alzheimer's disease, Down's syndrome and cognitive impairment (see p. 2, lines 28-30). Schenk teaches immunizing compositions comprising immunogenic fragments of A $\beta$  that are advantageous and can be presented by a display vehicle (e.g., by a virus or a bacteria) as part of an immunogenic composition (p.14, line 19 - p.16, line 17). Examples include peptide fragments that comprise the  $\beta$ -secretase cleavage site in Figures 19 and 20, including VKMDAEFRHD and ISEVKMDAE, which comprise SEQ ID NO: 5 (VKMDAEFRH) and residues 1 to 8 of SEQ ID NO: 1 (ISEVKMDA), respectively (as in claims 4, 5, 13, 14, 42, 45, 46 and 49). Immunization with such a composition to a subject in need thereof would inherently induce an immune response against the  $\beta$ -secretase cleavage site of A $\beta$ PP and would be expected to produce at least some antibodies directed against the  $\beta$ -secretase cleavage site of A $\beta$ PP and thus result in the blockade of  $\beta$ -secretase cleavage of A $\beta$ PP and the inhibition of the formation of amyloid  $\beta$ , as in claims 1-11, 13-15 and 42. Schenk also teaches that immunogenic peptides can be expressed as fusion proteins with a carrier peptide, such as a T helper cell epitope, which can serve to induce a helper T-cell response against the carrier peptide. The induced helper T-cells in turn induce a B-cell (i.e. antibody) response against the immunogenic peptide (see p. 29,

lines 20-28). Schenk discloses that the fusion proteins comprising the immunogenic peptide can then be linked to a core molecule, such as lysine, to form a multimer of fusion proteins. The multimer is represented by the formula  $2^x$ , in which x is an integer from 1-5, preferably x is 1, 2 or 3 (see p. 30, lines 13-22). For example, when x is 3, such a multimer has eight fusion proteins linked to a core molecule, as in the instant claims 2 and 3 regarding the number of function groups. Schenk teaches an example of the MAP4 (Multiple Antigen Peptide) configuration, in which 4 identical peptides have been produced on the branched lysine-containing core structure (see paragraph spanning pp. 30-31). Schenk teaches that such multiplicity greatly enhances the responses of B cells (see p. 30, line 29) as in claims 6 (overlapping APP epitopes), 7 (wherein the overlapping epitopes are identical), and 8 (core molecule is lysine). The T helper cell epitope, which would be part of the fusion peptide comprising the immunogenic peptide, which recites that the composition further comprises a molecule having adjuvant properties joined to said dendritic polymer, as in claim 9. Further, Schenk discloses that pharmaceutical compositions comprising the immunogenic peptides can be encapsulated in liposomes or micro particles for enhanced adjuvant effect (see p. 41, lines 29-33), as in claim 10. Schenk teaches that the patient is usually a human (see p. 37, lines 1-3), as in claim 15.

As evidenced by the prior art, the skilled artisan would have known that the immunogenic fragments of A $\beta$ PP, such as those disclosed in figures 19 and 20 can be used in treating or preventing diseases associated with amyloid deposits of A $\beta$  in the brain of a human patient. Thus, it would have been obvious to the person of ordinary

skill to try to make and use the claimed products and method in an attempt to provide an improved method of Alzheimer's disease, for example. This is because the artisan has good reason to pursue the known options within his or her technical grasp.

In the reply filed on 01 October 2007 regarding the previous rejection under 35 U.S.C. 102(b), Applicant asserts, "The 104 residue pBx6 polypeptide disclosed in Schenk is not displayed on a display vehicle as presently recited in the claims. New claims 44-50 to the antigenic peptide recite that it consists of 6-14 residues and therefore the 104 residue pBx6 polypeptide does not anticipate the new antigenic peptide claims 44-50. Regarding the peptide fragments disclosed in Schenk's Figs. 19 and 20, a closer reading of the disclosure in Schenk on page 102 relating to the epitope mapping experiment shown in Figs. 19 and 20 clearly shows that the peptides of Figs. 19 and 20 also have a GGK linker and are biotinylated. The GGK linker and biotin moiety on the biotinylated peptide are bound to streptavidin coated wells of 96 well plate. Accordingly, the GGK linker, biotin moiety and 96 well plate cannot be construed to be a display vehicle as recited in the present claims because it certainly cannot serve as an immunizing composition for administration to a patient. Therefore, Schenk's shorter peptide fragments cannot anticipate the present claims. New claims 44-50 to an antigenic peptide consisting of 6-14 residues also cannot be anticipated by Schenk's biotinylated peptide."

Applicant's arguments have been fully considered but they are not persuasive.

The Examiner agrees that the 104 residue pBx6 polypeptide does not anticipate the current claims since it is required that the peptide is 6-14 amino acids in length.

However, the Examiner does not agree that the presence of the GGK linker, biotin moiety and 96 well plate used in the experiments described in figures 19 and 20 renders the claims novel or unobvious over the Schenk document. Schenk teaches that immunogenic fragments of  $A\beta$  are advantageous for therapeutic use and can be presented as presented by a display vehicle (e.g., by a virus or a bacteria) as part of an immunogenic composition (p.14, line 19 - p.16, line 17). This segment of the document also teaches that the fragments require screening before use. This is exactly what is being performed in figures 19-20, i.e., the peptides are being screened. The skilled artisan would know that the peptides need not be used only in an assay for epitope mapping. Thus, without departing from the spirit of the invention, the artisan would know that the peptides disclosed in figures 19 and 20 could be used as part of the immunogenic compounds of the invention without the presence of the GGK linker, biotin moiety and 96 well plate and with the presence of a proper display vehicle. Since said peptides are VKMDAEFRHD and ISEVKMDAE, which comprise the instant SEQ ID NO: 5 (VKMDAEFRH) and residues 1 to 8 of SEQ ID NO: 1 (ISEVKMDA), respectively, as in the length limitations of the peptides in claims 1-11, 13-15 and claim 42. Similarly, without departing from the spirit of the invention, the artisan knows that the peptides themselves exist without the GGK linker, biotin moiety and 96 well plate, as in the instant claims. As stated previously, regardless of whether the  $A\beta$ PP peptide fragments

noted above are administered as immunizing agents, the immunization would inherently be expected to produce at least some antibodies directed against the  $\beta$ -secretase cleavage site of A $\beta$ PP.

The rejection of claims 11 and 12 under 35 U.S.C. 103(a) as being unpatentable over WO 00/72880 A2 by Schenk et al., in view of Frenkel et al. is maintained for reasons of record.

In the reply filed on 01 October 2007, Applicant asserts, "As no significant treatment-associated changes in A $\beta$  or A $\beta$ PP levels were observed from immunizing with a 104 residue region of A $\beta$ PP spanning the  $\beta$ -secretase cleavage site, Schenk's experimental results serve as a teaching away from using or displaying an antigenic peptide that spans the  $\beta$ -secretase cleavage site in an immunizing composition. Accordingly, one of ordinary skill in the art would not be led to arrive at the presently claimed invention by the combination of Schenk's and Frenkel's teachings."

Applicant's arguments have been fully considered but they are not persuasive. The Schenk reference is not applied as a primary reference for its teaching of the 104 residue pBx6 polypeptide; rather, it is applied for its teachings of the shorter peptides set forth above. Thus, it is irrelevant that the longer polypeptide did not result in significant changes in A $\beta$  or A $\beta$ PP levels and the Schenk reference does not teach away from the claimed invention. Therefore, the rejection is maintained.

***Conclusion***

Claims 1-15, 42 and 44-50 are rejected. Claims 27, 29, 38, 40 and 43 are objected to as being dependent upon a rejected base claim, but would otherwise be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregory S. Emch/

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Patent Examiner  
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10 January 2008

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